Applicant: Roche Diagnostics Corp., US

Method for checking the fitness for purpose of analysis elements

The invention relates to a method for checking the fitness for purpose of analysis elements, in which method a check is performed whether a measured control value for at least one control parameter of a checked analysis element is within a tolerance range. Furthermore, the invention relates to a corresponding evaluation device.

For the qualitative and quantitative analysis, by means of chemical and biochemical processes for the analysis of sample materials, in particular liquid samples, in particular of a body liquid of human beings or animals, so-called substrate-based rapid tests are used to a large extent, in laboratories specialized on this, but in particular also for the use outside of fixed laboratories. These substrate-based rapid tests are based on a specially developed dry chemistry process, and can be performed easily and without problems even by nonexperts, in spite of the complex reaction occurring in many cases, using sensitive reagents.

For this, analysis elements are used which have reagents embedded in one or more test layers. For the execution of

a reaction, the analysis element is brought into contact with the sample. The reaction of sample and reagent leads to a change of the analysis element, which change is characteristic for the analysis and can be evaluated visually or by means of an evaluation device (in most cases, reflection-photometrically). The analysis elements are also designated as test elements.

Generally, the evaluation device is appropriate for the evaluation of a very certain type of analysis elements of a certain manufacturer. For this, the analysis elements and the evaluation device are components which are mutually adjusted to each other, as a whole, they are commonly designated as analysis system.

A plurality of different analysis element types are known, differentiated by the measuring principle (e.g. optical or electrochemical) and the used reagents, as well as by their structure, in particular by the arrangement and the fastening of the test layers. In particular, strip-shaped analysis elements (test strips) are common, consisting of an oblong plastic stripe ("basic stripe") and at least one test layer fixed to it. For another common analysis element type, a plastic frame is used, enframing at least one test layer.

A known example for substrate-based rapid tests are test elements for the determination of the blood glucose content for diabetics. Other known embodiments of stripe-shaped diagnostic test elements are, e.g., one-field- or multi-field test stripes for urinanalysis and different test papers. Analysis elements to be evaluated with an apparatus, e.g. electrochemically or optically, in particular analysis elements to be evaluated photometrically, are comprehensively described in the prior art,

and are known to the persons skilled in the art in a plurality of embodiments.

It is known that the analytic function of the analysis elements can be damaged by environment factors as e.g. light, temperature or humidity. Such damages can lead to fault in measuring when used; this can have dangerous consequences for a diagnosis basing upon this, or can render the analysis elements unusuable.

In the presence of light-sensitive, temperature-sensitive or humidity-sensitive compounds, photometrically evaluated analysis elements can change, even before use, their dry color in such an extreme way that this can be recognized by an alert user. In these cases, the analysis elements can be manually segregated. However, the visual assessment is difficult and requires experience. Moreover, due to the methodical difficulties, this is rarely performed, or simply forgotten, in particular by nonexperts.

In order to protect the analysis elements from the impact of light beams, the access of humidity, dirt, germs, dust, as well as from mechanical deterioration, or in order to store them under sterile conditions, the analysis elements are generally packaged. For this, the analysis elements can be packaged individually, or be comprised in a common packaging or in a storage container. However, the packaging does not offer a 100% protection. For example, it can be damaged during fabrication, transport or improper storage. However, the most important factor is that the packaging offers only very little protection against temperature influences and that it does guarantee only little or no protection against aging effects. The aging process proceeds in an increased way after a package or a storage container has been opened, so the aging

of analysis elements in this period of time should receive special consideration.

Thus, for checking the fitness for purpose of an analysis element, for photometric measuring systems it is known, in the prior art, before applying the sample to be measured, to determine the so-called dry blank value of the measuring field, i.e. the remission value of the analysis element, without the sample applied. This dry blank value is compared to a comparative value; the analysis element is rejected if the dry blank value serving as control parameter is not within a given tolerance range.

For this known procedure, only a very inaccurate check is possible, as the measuring devices used for the evaluation of the analysis elements show individual tolerances during their production, and as the differences between the devices even amplify during service life, e.g. due to changes of the measurement device, in particular for optical measurement systems. These changes can be caused by mechanic charges leading to misadjustment, aging of the illumination systems (e.g. light emitting diodes) or dust deposits on the optical elements. Furthermore, batch fluctuations influencing the dry blank value result in the fact that only inaccurate checks are possible, unless these batch fluctuations are considered by batch-specific information which is taken over from the analysis elements or their respective packaging into the evaluation device.

So far, no methods for checking or monitoring of the fitness for purpose are known for electrochemical analysis elements, in opposite to photometric analysis elements.

From the document US 4,832,488, it is known to consider the aging effects of optical analysis elements, which can lead to a change of the calibration curve used in the analysis, by parameters describing the aging process. The parameters are determined by optical measurements of analysis elements, among which also is, in some case constellations, the measurement of the dry blank value; the rectification of the calibration using these parameters leads to an improved measuring accuracy of the analysis. However, this procedure is sophisticated with respect to its practical application, and does not include any control of the fundamental fitness for purpose of the analysis elements.

Test stripe elements are known from document DE 2800225 A1, which show a reference field with comparison or compensation paper pieces. These are exposed, just as the proper test field, to radiation of different wavelengths, measuring the reflecting power. The changes caused by samples on the reference field are detected; with this, the influence of the measurement field caused by characteristics of the sample, not based on the concentration of the analyte, is compensated. This is a correction of sample-related changes of the measurement conditions of an analysis device. There is no control of the fitness for purpose of an analysis element.

Taking into account this state of the art, the object of this invention is to provide a simple and reliable method for checking the fitness for purpose of analysis elements.

According to the invention, this object is achieved by a method with the features of the appended claim 1. Preferred embodiments and further developments of this in-

vention can be taken from the claims 2 - 20, and the subsequent description with the corresponding drawings.

A method according to the invention, for checking the fitness for purpose of analysis elements, in which method a check is performed whether a control value measured for at least one control parameter of a checked analysis element is within a tolerance range, comprises the following steps:

a) In a first step, a first standard reference value is determined in a reference value measurement, using a reference control means. The reference control means provides a standardized reference value for the control parameter.

b) In a second step, the control parameter of a first analysis element is determined as control reference value.

c) In a third step, the quotient from the control reference value and the first standard reference value is calculated and set as first reference quotient for analysis elements measured later.

d) In a fourth step, the control parameter of a second analysis element is determined as control value for the second analysis element to be checked.

e) In a fifth step, the quotient from the control value and the first standard reference value is calculated as the control quotient.

f) In a sixth step, the deviation between the control quotient and the first reference quotient is determined.

g) The checked second analysis element is rejected if the deviation is not within a given tolerance range.

Below, the invention is described, without limiting the universality, using the example of photometrically evaluated analysis elements. The explained principles can easily be applied to other analysis elements, e.g. electrochemical ones.

For electrochemical analysis elements, an electronic measured quantity, appropriate for the performance of the check, can be used. For example, a blank value measurement with an AC voltage, for which the impedance or the phase shift provide the control parameter, can be considered for this. Other possible control parameters are conductivity, capacitance, inductance, decay times, frequency dependencies, or other functional correlations of electronic measured quantities which can be expressed in characteristic curves; e.g. a characteristic depending on current, voltage or frequency. For cases in which the proper electrochemical analysis element itself does not show an appropriate control parameter, it is possible, in order to enable the possibility of measuring, to add an additional component to the analysis element, providing a characteristic which allows measurement and which is appropriate for the check purposes according to this invention.

Thus, the method as according to this invention essentially comprises two aspects. According to the first aspect, changes of the optical measurement system are moni-

tored. For this, a reference value is measured using a standardized reference surface, e.g. a white standard measurement, providing a standardized reference value for the control parameter. No sample material is applied to the reference surface. In the context of this invention, an optical measurement value, in particular a remission value, is a very appropriate control parameter. The first standard reference value determined by this checks the current state of the evaluation device, e.g. of the optical measurement system, and can be used for a post-calibration of the evaluation device; however, this is not necessary in the context of the invention; it is sufficient to use the standard reference value as a reference value for subsequent measurements.

The second aspect refers to the check of the fitness for purpose of individual analysis elements, which could be impaired by e.g. damaging influences or aging. For this, the control parameter of a first analysis element is determined at the reactive measurement field before applying the sample material, using it as control reference value for analysis elements measured subsequently. For this purpose, the quotient from the control reference value of the first analysis element and the first standard reference value is calculated, and the quotient is set as the first reference quotient. For the subsequent check of a second analysis element to be checked for its fitness for purpose, the control parameter is determined at the reactive measurement field before applying the sample material, i.e., for example, the dry blank value of the second analysis element is determined as control value, and the quotient of the determined control value of the second analysis element and the first standard reference value is calculated as the control quotient. Using the deviation between the control quotient and the

first reference quotient, it can then be checked whether the checked second analysis element is fit for purpose, or, if the deviation is not within a given tolerance range, if it must be rejected due to deterioration.

With the method according to the invention it is possible to check easily and reliably, before performing an analysis, without expensive re-calibration processes, whether an analysis element can be used for the performance of an analysis, or whether it must be rejected due to the existence of deterioration, in particular in case of aging after a package has been opened.

For this method, it is presupposed that the first analysis element which has been used to determine the control reference value, is undamaged and fit for purpose. The fitness for purpose of the first analysis element is not controlled by the method according to this invention. However, this can be checked, at least in a coarse way, according to the method known in the state of the art, using the dry blank value of the first analysis element; if the control reference value determined for the first analysis element is not within a given tolerance, the first analysis element is not fit for purpose.

The method according to the invention principally works without the reference measurement of step a), too. However, step a) makes the method more sensitive, as it considers the differences of different analysis devices, e.g. deviation due to the manufacturing of the optical measuring systems. However, the coarse check of the first analysis element is not the object of the invention; the invention is focussed on the check of the analysis elements following the first analysis element, proposing the method described above.

Thus, the method according to the invention is advantageous with respect to an additional aspect, in particular for such application cases for which the first analysis element and the second analysis element, the one to be checked, are comprised in a package or in a storage container, which contains further similar analysis elements, showing a long-time packaging common to all analysis elements. For this, according to another advantageous feature, the analysis elements in the package may be protected additionally and individually by an individual packaging means.

In these application cases, the common long-time packaging guarantees, with a high degree of safety, that the analysis elements contained therein, and thus, the first analysis element, are not deteriorated, except for possible deterioration caused by temperature influences, which can be determined by means of the known blank value tolerance measurement. After opening the long-time packaging, the danger of damaging individual analysis elements contained in the package by improper handling, is high. However, a deterioration of the fitness for purpose of individual analysis elements after opening the long-time packaging, can advantageously be recognized by the check according to this invention.

The invention has the advantage of enabling a simple and reliable check of analysis elements. Another advantageous feature is the fact that one or more of the method steps are performed automatically, i.e. in a user-independent way. It must be noted that the sequence of the steps according to the invention can be modified conveniently - e.g., the order of the steps a) and b) can be interchanged - thus, the designations "first" step etc. only

serve for the differentiation of the individual method steps without determining the sequence; the method step sequence given in claim 1, however, is a preferred embodiment.

Furthermore, the terms "first analysis element" and "second analysis element" do not restrictively designate the first measured analysis element (of a package), or the immediately subsequent analysis element, respectively, but designate merely a conceptual differentiation. The first analysis element is the one used for the determination of the standard reference value. This is preferably, but not necessarily, the first analysis element in the package. The second analysis element is one of the analysis elements checked subsequently, or checked in relation to the first analysis element. These are preferably, but not necessarily, all analysis elements following the first analysis element.

The invention will subsequently be explained in detail with the help of an examplary embodiment shown in the figures. The characteristics described can be used individually or in combination, in order to create preferred embodiments of this invention.

Fig. 1 shows an analysis element in the shape of a test stripe.

Fig. 2 shows a package with test stripes contained in a storage container.

Fig. 1 shows an analysis element 1 in the shape of a test stripe which can be inserted into an evaluation device not shown; the evaluation device and the analysis elements adapted thereto form an analysis system. The analysis element comprises an elastic basic layer 2, normally

consisting of a plastic material. It carries a test field 3, onto which a sample liquid to be analyzed has to be applied. During the analysis, chemical reactions between the sample liquid and the reagents contained in the test field 3 take place. A resulting, optically provable change can be detected reflection-photometrically.

Many embodiments of test elements are known, differentiated e.g. by the type of the chemical detection reaction, the layer structure in the test field, the optical measurement method, and the number of test fields 3 on a test stripe. All previously known test stripes are appropriate in the scope of the check method according to the invention.

The fitness for purpose of the analysis element 1 can coarsely be checked with a so-called dry blank value measurement of the test field 3, i.e. an optical measurement of the test field 3 without the application of sample liquid. For this, the analysis element 1 is inserted into the evaluation device without a preceding application of sample liquid, and the dry blank value is measured. If the dry blank value, serving as control parameter, is within a given tolerance range, which range can be determined batch-specific, if necessary, there is an increased probability for analysis element 1 to be not deteriorated, and thus fit for purpose. Subsequently, the analysis element is taken off the evaluation device, the sample liquid is applied to it, and then it is re-inserted into the measurement unit of the evaluation device for performing the proper analysis. The evaluation device can conveniently be designed to allow the application of the sample without the need to remove the analysis element 1 once again.

In order to perform the check method according to the invention, the analysis element 1 advantageously comprises, in addition to the test field 3 serving for the check of its fitness for purpose and for performing the analysis, an integrated reference control means, providing a standardized reference value for the control parameter, e.g. the remission value. The reference control means does not suffer any change caused by the sample material; it is non-reactive, and no sample material adheres to it. The reference control means is embodied in the shape of a reference field 4, providing a standardized reference value for the remission. In a preferred embodiment, the reference control means consists of a white plastic foil or contains such a foil.

The remission value of the reference field is preferably high, e.g. 80%, in order to allow a high measured value for the remission control parameter, and thus, a relative high accuracy of measuring. In the framework of the invention, however, there are no very high requirements to the reference field 4, serving as reference control means. For example, a less remitting gray surface can be considered, too; the remission value of the reference field 4 does not need to be stable over a long period of time. However, it is preferred if the characteristics of the reference field 4 are, to a large extent, independent from environment conditions such as temperature and humidity.

Fig. 1 shows the reference field 4 as a specially designed part of the analysis element 1. However, due to the uncritical requirements to the characteristics of the reference field 4, as explained above, it is also possible to use a section of the analysis element 1 as reference control means, which is not specially designed, e.g.

a part of the surface of the preferably white plastic the test stripe or its basic layer 2 is made of. In these cases, the marking of reference field 4 in Fig. 1 only illustrates which place of the analysis element 1 serves as reference control means, without an existing difference of this area with respect to neighboring areas.

The reference field 4 can be an integrated component of the analysis element 1, as shown in Fig. 1. However, it is also possible to provide the reference field 4 on a separate reference test stripe not equipped with a test field 3, being added to the evaluation device and/or to a package or batch of analysis elements 1. In other embodiments, the reference field 4, or the reference control means in general, can be an integrated component of the corresponding evaluation device.

The reference field 4 serves as a reference value allowing to consider the current state of the evaluation device or its optical system. It allows the detection of fluctuations of the measurement conditions, caused by the apparatus. For this, as a first step of a reference value measurement, a first standard reference value W1 of a white standard value of e.g. 80% remission is measured for reference field 4. For this, the analysis element 1 is brought into a position into the evaluation device where not the test field 3, but the test field 4 is measured instead.

The white standard value W1 only results in a fixed and constant value for a certain measuring apparatus with defined and constant measuring properties. This cannot be realized in practice, in particular not in measuring devices outside of laboratories, resulting in the fact that the white standard value W1 is submitted to apparatus-

caused fluctuations of the evaluation device (and, possibly, to fluctuations with respect to the characteristics of the reference field 4). However, this is not disadvantageous in the framework of the invention; exactly by referencing to a white standard, using the quotient calculation according to this invention, apparatus-caused changes, which can also arise in short term, can be considered.

After that, or, if necessary, also before that, the dry blank value L1 of the test field 3, brought into the measuring position in the evaluation device, is determined in a second step. For this, it can optionally be checked, at the same time, whether the dry blank value L1 is within a given or, if necessary, charge-specific tolerance range. In the exemplary embodiment it is presupposed that the dry blank value of analysis elements 1 which are fit for purpose shows a remission between 55 % and 65 %, and a remission of 60 % for the actual measurement.

In a third step, a quotient from the control reference value L1 measured for the first analysis element and the first standard reference value W1 is calculated and set as first reference quotient Q1 for analysis elements measured later. Thus, in the supposed example, the first reference quotient Q1 is 60/80 = 0,75.

The first analysis element, which has been used for calculating the first reference quotient Q1, can subsequently be used for performing an analysis. For this, it is taken off the evaluation device, the sample to be analyzed is applied to the test field 3, and the analysis element is inserted into the evaluation device for analy-

sis; or, the sample is applied to the analysis element left in the evaluation device.

If a second analysis element is used, first the control value L2, i.e. the dry blank value of test field 3 of the second analysis element, which is to be checked, is determined. This dry blank value L2 is divided by the first standard reference value W1, forming the control quotient Q2; after that, the deviation Δ between the control quotient Q2 and the first reference quotient Q1 is checked. The checked second analysis element is rejected if the deviation Δ is not within a given tolerance range.

The decision whether the deviation Δ is outside a given tolerance range or not, can be made, e.g. using the quotient Q1/Q2, i.e. the relative difference between the first reference quotient Q1 and the control quotient Q2, using an (absolute) difference Q1-Q2 or using a functional or parametrical evaluation of the deviation Δ,.

If, for example, the dry blank value L2 in the supposed example is 56.4%, and the tolerance range for the admissible deviation is a relative Δ 6 % , referred to the first reference quotient Q1, or an absolute 0.045, referred to the difference of Q1 and Q2, the control quotient Q2 of 56.4/80 = 0.705 of the second analysis element is just within the admissible range, allowing the second analysis element to be used for analysis. However, if the measurement of the control value L2 results in a dry blank value of 50% for the second analysis element, a control quotient Q2 of 50/80 = 0.625, and a deviation Δ of a relative 16 % or an absolute 0.125 come out. In this case, the checked second analysis element in question is not admitted to be used for analysis and must be rejected.

The tolerance range for the admissible deviation Δ can be batch-specific for the current batch of analysis elements. This can be realized by providing the analysis elements or their packaging with a bar code, which can be read by the measuring device and be considered for the check or for the analysis. A modification of this can be the storage of a set of tolerance ranges in the evaluation device, from which one value is selected for the batch in question via the bar code readout.

The measurement of the standard reference value W1 could principally be performed for each analysis element. However, this is not necessary in the framework of the invention, so time is saved if the measurement is only performed in case of necessity.

For some analysis elements, in particular for test elements for a substrate-based rapid test for the qualitative or quantitative analysis of components of a solid or liquid sample, in particular of body liquids of human beings or animals, in particular for the determination of the blood glucose content, the checked second analysis element may be rejected in step g), if the control quotient Q2 is smaller, by more than a given percental value or more than a given difference value, than the first reference quotient Q1. The reason for this is that it was found out in the framework of the invention, that, in particular for the test elements mentioned above, aging and deterioration influences lead, in most cases, to a decrease of the remission value, and thus, to a decrease of the control quotient Q2 as compared to the reference quotient Q1, and that, for this reason, the decrease can be used for checking purposes.

According to another preferred feature, in particular for the test elements mentioned above, it may be provided that in case of the determination of a given deviation Δ in step g), the control value L2 determined in step d) is used as new control reference value according to step b), calculating a new reference quotient from this according to step c), and that this new reference quotient is used as basis for checking further analysis elements according to steps d) to g). A given deviation Δ in this respect, which leads to the replacement of the first reference quotient Q1 by the later measured control quotient Q2, replacing it for the purpose of subsequent checks, can be the observation that the control quotient Q2 determined in step e) exceeds the current (first) reference quotient Q1 by more than a fixed limit value δ.

In the example mentioned above, for example, the measurement of a control value or dry blank value L2 of an analysis element to be checked, of more than 61.8 %, leads to a control quotient Q2 bigger than 0.7725, and thus to the replacement of the first reference quotient Q1 of 0.75 by the control quotient Q2, if a value of 3 %, referred to the first reference quotient Q1, or 0.0225 as deviation of Q1, is given for the admissible limit value δ. In an additional advantageous embodiment, it may be provided that the limit value δ is batch-specific for the current batch of the analysis elements.

An increase of the control quotient Q2 as compared to the first reference quotient Q1 may result if the optical measuring system has been cleaned, or if any other conceivable action, with influence on the check or the analysis, has been taken. This can be recognized using the method according to the invention and can be consid-

ered for the check of the fitness for purpose of the analysis elements.

It must be noted that the exemplarily explained quotients and differences can also be calculated vice versa, i.e. with commuted dividend and divisor, or with commuted minuend and subtrahend.

The method according to the invention is preferably used in cases for which the first analysis element and the second analysis element, the one to be checked, are comprised in a package or in a storage container, which contains further similar analysis elements, showing a long-time packaging common to all analysis elements. Fig. 2 schematically shows such a package 5. One of the contained analysis elements 1 is shown schematically. The analysis elements comprised in a package 5 are enveloped by a long-time packaging 6, providing a safe protection. The long-time packaging 6 can be a high-tenacity welded foil, or a tube-shaped container made of plastic or metal, e.g. aluminum.

Each of the analysis elements 1 contained in the package 5, may be protected by an individual packaging element. In this case, the long-time packaging 6 ensures a secure storage over a long period of time, or a secure transport, respectively. In order to use the analysis elements 1 contained in package 5, the end user first opens the long-time packaging 6; the analysis elements 1 contained therein are then consumed one by one. In the time between the opening of the long-time packaging 6 and the use of a certain analysis element 1, the individual packaging elements ensure the required minimum protection. The method according to the invention allows to check whether the minimum protection is actually complied with, and whether

all analysis elements 1 or an individual analysis element 1 have deteriorated with respect to their fitness for purpose after the opening of the long-term packaging 6.

It is also known to arrange the analysis elements 1 in the long-time packaging 6, not in a loose way, but in a storage container 7, which does not only provide a packaging function, but which is also able to provide a functional part for the intended use of the analysis elements 1. The arrangement of various storage containers 7 in a common long-time packaging 6 is also possible. Examples for storage containers and removal devices can be found in the documents DE 19854316 A1, EP 1022565 A2, US 4,615,462, US 4,834,234, US 5,645,798 and US 5,720,924.

Fig. 2 exemplarily shows such a storage container 7 in the form of a magazine, in the chambers 8 of which the analysis elements 1 are arranged. The openings 9 of the chamber 8 are closed by sealing foils 10 which represent individual packaging units; these are punctured for the removal of a analysis element 1 from a chamber 8 of the storage container 7; for this, the sealing foils 10 of the other analysis elements 1 not to be removed remain undamaged and supply protection for the analysis elements 1 remaining in the respective chamber 8.

The storage container 7, arranged in the shape of a magazine, is conceived for the use in an evaluation device. Corresponding means for the exact positioning and removal can be provided for the incorporation of a storage container into an evaluation device, for which, e.g., an analysis element can be removed from a chamber by means of a plunger.

In the framework of the invention it is supposed that the analysis elements 1 are fit for purpose until the long-time packaging is opened, or that a possible deterioration, e.g. by a temperature effect which affects all analysis elements, can be detected using a conventional checking method. Generally, the opening of the long-time packaging 6 is effected immediately before the use of the first analysis element 1 contained therein. Thus, according to a preferred embodiment of the invention, it is proposed to choose, for step b), the analysis element 1 which is removed first from a package 5 or a storage container 7 contained in package 5. For example, the evaluation device can be designed in a way that it automatically performs the steps a), b) and c) according to the invention, when a new package 5 is used, when a first analysis element 1 of a package 5 of a storage container 7 is used, or when a long-time packaging 6 is opened.

Furthermore it is advantageous to repeat the steps a) to c), if a change which potentially influences the measured value, e.g. a cleaning of the optical system, was performed on the evaluation device which performs the control measurement or the analytical measurement, respectively. For example, a repetition of steps a) to c) can be activated automatically if the evaluation device registers, by means of a control switch, that a cover of the evaluation device which enables access to the optical system, was opened, as in this case a cleaning process has probably been performed.

The subsequent tables 1 and 2 show the results of practical trials of the invention. During these, test stripes serving for the determination of the blood glucose content, were checked. The test stripes suffered artificial aging by submitting them to 80 % relative humidity. For

this, the high humidity serves as increased load, accelerating the aging processes. Corresponding trial results were obtained during tests with increased temperature, or under real conditions with prolonged aging conditions.

Table 1 states the load results for 80% relative humidity with a first, fixed standard reference value W1. t is the duration of the humidity load for 80% relative humidity, expressed in hours. The standard reference value W1 measured in the first step a), the control reference value L1 measured in the second step b), and the control value L2 measured in the fourth step d) are given arbitrarily in mV. In practice, other units may occur, too, e.g. mA, light intensity or a percental remission value. The first reference quotient Q1 formed in the third step c) and the control quotient Q2 formed in the fifth step e) are stated in percent. The last column of the table shows the deviation Δ between the control quotient Q2 and the first reference quotient Q1, determined in the sixth step f); in the shown example, the difference of these values has been chosen.

It can be seen that the aging effects increase and the control quotient Q2 decreases with increasing load time. The deviation Δ between the control quotient Q2 and the first reference quotient Q1 increases accordingly. If the determined deviation Δ exceeds a given limit value, it is possible to determine by this that the test element intended for an analysis is not fit for purpose. In table 1, such a limit could be set for a Δ bigger than ± 6, for example.

Table 1

t in h	a) W1 in mV	b) L1 in mV	c) Q1 = L1/W1 in %	d) L2 in mV	e) Q2 = L2/W1 in %	f) Δ = Q2-Q1
0	88.5	67.6	76.4	-	-	-
48	-	-	-	65.8	74.4	-2.0
96	-	-	-	60.3	68.1	-8.3
144	-	-	-	56.7	64.1	-12.3
192	-	-	-	53.4	60.3	-16.1

Table 1: Aging test for a relative humidity of 80% with a fixed control reference value W1.

Table 2 shows a corresponding aging test, for which, in opposite to table 1, the standard reference value W1 is not only determined at measurement start, but is newly determined for every time-related control stage. A corresponding variation of the standard reference value W1 can also result from the fact that different analysis devices are used, which are different with respect to their optical and measuring-technological characteristics.

In table 2 it can also be recognized that the variation of the standard reference value W1, protocolled here for test purposes, is low, and that it is not submitted to the aging process. Thus, during the practical use of the invention, it is not necessary to re-determine the standard reference values W1 each time, in order to recognize an aging process due to the change of the control values L2.

Table 2

t in h	a) W1 in mV	b) L1 in mV	c) Q1 = L1/W1 in %	d) L2 in mV	e) Q2 = L2/W1 in %	f) Δ = Q2-Q1
0	88.5	67.6	76.4	-	-	-
48	88.1	-	-	65.8	74.7	-1.7
96	87.8	-	-	60.3	68.7	-7.7
144	88.2	-	-	56.7	64.3	-12.1
192	88.3	-	-	53.4	60.5	-15.9

Table 2: Aging test for a relative humidity of 80% with change of control reference value W1.

The effect of the aging with respect to the falsification of the measurement results for the glucose concentration c is shown in table 3.

Table 3

c for t = 0 in mg/dl	t in h	c (t) in mg/dl	Δ c in %
87.3	48	86.8	-0.6
87.3	96	79.4	-9.0
87.3	144	74.7	-14.4
87.3	192	71.3	-18.3
201.7	48	207.6	2.9
201.7	96	194.6	-3.5
201.7	144	183.9	-8.8
201.7	192	172.0	-14.7
343.9	48	350.1	1.8
343.9	96	332.6	-3.3
343.9	144	313.6	-8.8
343.9	196	299.3	-13.0
504.8	48	510.9	1.2
504.8	96	474.8	-5.9
504.8	144	446.2	-11.6
504.8	196	422.4	-16.3

Table 3: Glucose values after aging

It can be recognized that in case of a load time t of more than 96 hours, for a relative humidity of 80 %, deviations of more than 5% occur. If a tolerance range for the deviation Δ of ±6 is chosen accordingly for the tables 1 and 2, the aged test elements which are no longer fit for purpose, can be recognized and segregated, using the method according to the invention.

The method according to the invention offers essential advantages as compared to the state of the art, for which the control value is only compared to a fixed limit

value, pre-adjusted on the device. The differentiation potential as according to the state of the art is essentially lower, so that glucose value deviations between loaded and unloaded samples can only be recognized if they correspond to 30% or more. Thus, the known methods cannot even determine the deviation of the glucose values of about 15%, occurring after a load time of 192 hours (see table 3).

The invention allows a simple and reliable check of the fitness for purpose of analysis elements. It is particularly advantageous if the photometric inspection of the dry blank value is effected user-independently for each analysis element, i.e. self-acting and automatically, and that the decision exactness is essentially increased by referencing the measured value. In order to take into account the state of the optical system of the evaluation device, thus becoming independent from variations, the current state of the optical system of the device is referenced to a white standard by means of a comparative measurement. The dry blank value of controlled analysis elements is also referenced to the white standard, effected by means of a quotient formation. The control quotient of a checked analysis element is compared to a first reference quotient. The first reference quotient is updated in case of necessity, so that the real state of the optical system of the evaluation device and the batch-depending target value of a package of analysis elements are always considered currently. By this, a very fine recognition characteristic for deteriorated analysis elements is obtained.

In order to check the functionality of the checking method as according to the invention, in a corresponding evaluation device, deteriorated and not deteriorated

analysis elements can be inserted alternately into the evaluation device, thus testing the reaction of the evaluation device. If it works properly, it will, according to the order of analysis elements inserted for the testing of the device, accept these analysis elements for measurement, or reject them, as well as perform, if necessary, a new measurement on a reference field.

List of reference signs

1	Analysis element
2	Basic layer
3	Test field
4	Reference field (reference control means)
5	Package
6	Long-time packaging
7	Storage container
8	Chamber
9	Opening
10	Sealing foil
L1	Control reference value (dry blank value of the first analysis element)
L2	Control value (dry blank value of the second analysis element)
Q1	First reference quotient
Q2	Control quotient
W1	First reference standard value (first white standard)
Δ	Deviation
δ	Limit value
t	Time
c	Concentration